REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ORGANIZATION.

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
20/01/2018	Poster	01/20/2018-01/21/2018

4. TITLE AND SUBTITLE
A Team Approach: Giant Cell-Rich Primary Bone Sarcoma

5a. CONTRACT NUMBER

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Krause, Capt Katherine

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
59th Clinical Research Division
1100 Willford Hall Loop, Bldg 4430
JBSA-Lackland, TX 78236-9908
210-292-7141

8. PERFORMING ORGANIZATION REPORT NUMBER
17596

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
59th Clinical Research Division
1100 Willford Hall Loop, Bldg 4430
JBSA-Lackland, TX 78236-9908
210-292-7141

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release. Distribution is unlimited.

13. SUPPLEMENTARY NOTES
Texas Sociery of Pathologists Annual Meeting, Houston, Tx, Jan 20-21, 2018

14. ABSTRACT
Bone neoplasms represent a particularly challenging subtype for pathologists, with more of a reliance on radiologic features than with other tissue types. Relatively new advances, such as histone immunohistochemistry, have been proposed as useful adjuncts. Clinical features may also play an important role in reaching the correct diagnosis. The following case demonstrates the importance of a multidisciplinary approach for a unique soft tissue neoplasm.

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			Clarice Longoria
			UU		19b. TELEPHONE NUMBER *(Include area code)* 210-292-7141

A Team Approach: Giant Cell-Rich Primary Bone Sarcoma Diagnosis

Authors: Katherine A. Krause, MD and Kevin J. Krauland, MD

Approved for public release. Distribution is unlimited.

Abstract

Bone neoplasms represent a particularly challenging subtype for pathologists, with more of a reliance on radiologic features than with other tissue types. Relatively new advances, such as histone immunohistochemistry, have been proposed as useful adjuncts. Clinical features may also play an important role in reaching the correct diagnosis. The following case demonstrates the importance of a multidisciplinary approach for a unique soft tissue neoplasm.

Case Report

A 23-year-old male presented to his primary care manager with residual knee pain after minimal trauma. Radiographs demonstrated a lesion suspicious for a primary bone tumor within the metaphysis of the right femur, and a giant cell tumor of bone was diagnosed via bone biopsy. During the subsequent excision and curettage, an intraoperative consultation confirmed an unusual giant cell neoplasm that was favored to be benign. In less than three months, the patient returned to his surgeon with increasing pain and a growing mass at the previous surgery site. His provider ordered a PET CT, revealing an FDG-avid mass in the right femur as well as in his right lung. Biopsies of both sites were giant-cell rich, and a bone and soft tissue expert diagnosed giant cell-rich sarcoma. The patient underwent chemotherapy followed by above the knee amputation of his right lower extremity. The patient's care was ultimately transferred to a cancer center where he is currently undergoing further treatment.

Histopathology

The two main cell types in giant cell tumor of bone (GCTB) are stromal cells and giant cells, with the mesenchymal cells representing the neoplastic population. Mitoses may be significant and pseudoanaplastic changes can be seen[1,2]. Additionally, reactive bone often rims these lesions.

Giant cell-rich sarcomas demonstrate malignant cells that can be epithelioid to ovoid to spindled with hyperchromatic and vesicular nuclei. Prominent nucleoli can be seen, as well as pleomorphism, increased mitotic activity, and atypical mitoses. The giant cells lack features of malignancy[3].

In this case, the spindled cells demonstrate hyperchromasia and polymorphism.

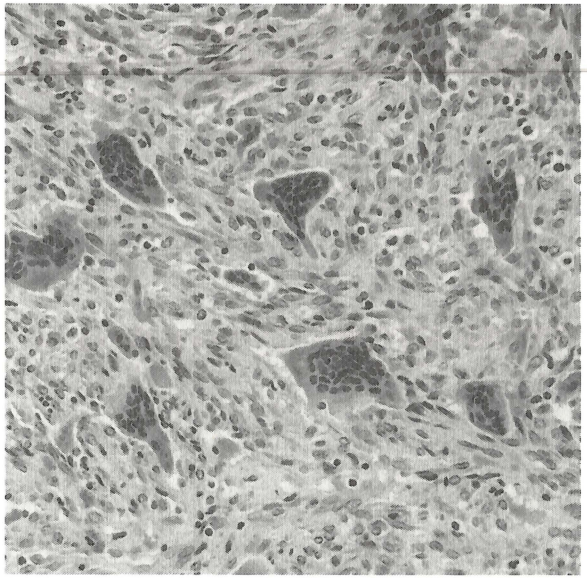
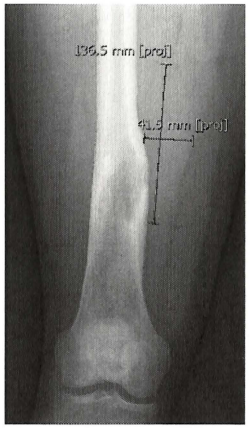
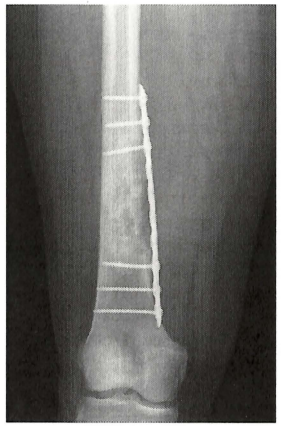


Figure 1. Osteoclast-like giant cells with spindled stromal cells.





Figures 2, 3. Initial radiograph and radiograph of recurrence.

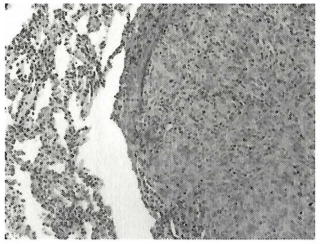


Figure 4. Giant cell lesion within lung

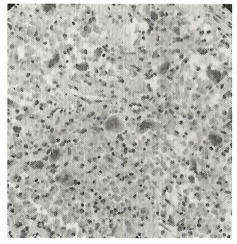


Figure 5. GCTB status-post chemotherapy.

Discussion

GCTB is a unique entity typically occurring in the epiphysis of long bones that recurs in up to 50% of patients treated with curettage[2]. Lung metastases are also well-documented, occurring in about 2% of patients[1]. Thus recurrence and lung metastases alone do not absolutely indicate malignancy. Rather, a multidisciplinary approach is paramount to achieving the right diagnosis.

In this case, the recurrence was rapid and aggressive. Lung metastases typically occur three to four years after diagnosis, and again, this patient had a much more rapid occurrence of three months[2]. The clinical team recognized the patient's signs and symptoms, leading to imaging, biopsy, and appropriate treatment.

The radiologists were also invaluable. The diagnosis of a bone tumor often starts with the plain film. The plain film of the patient's recurrence demonstrated a Codman triangle, and in GCTB there is minimal to no periosteal reaction. A periosteal reaction thus suggests a different process. Additionally, the nuclear medicine study further swayed the clinical team toward a more aggressive approach.

The metaphyseal location in this patient, while unusual, is not unheard of. Chow found that of four patients with metaphyseal giant cell tumors at his institution, no evidence of disease was found after treatment[4].

Histone gene mutations have been identified in various neoplasms, and in GCTB, the mutated gene found in over 90% of cases is H3F3A. Non-GCTB entities do not commonly express the mutation; Righi et al. found no H3F3A mutations in 28 primary giant cell-rich sarcomas of bone. Ultimately, a bone and soft tissue pathologist ordered an immunohistochemistry histone marker, H3G34W, for this case, which was found to be negative[5].

Given this constellation of findings, including rapid and aggressive recurrence, concerning radiologic features, negative histone immunohistochemistry, increased mitotic figures, and pleomorphic, hyperchromatic spindled cells, an expert pathologist diagnosed giant cell-rich primary bone sarcoma.

The pathologist did not diagnose solely on histology, but instead factored in the various clinical factors, resulting in an entirely different treatment plan for the patient. A multidisciplinary approach helped this diagnosis to be reached in a more timely manner, allowing for earlier treatment and potentially a better outcome for the patient.

References

1. Reith JD. Bone and Joints. In: *Rosai and Ackerman's Surgical Pathology*. 11th ed. Philadelphia, PA: Elsevier; 2018:1740-1809.

2. Righi A, Mancini I, Gambarotti M, et al. Histone 3.3 mutations in giant cell tumor and giant cell–rich sarcomas of bone. *Human Pathology*. 2017;68:128-135. doi:10.1016/j.humpath.2017.08.033.

3. Liegl-Atzwanger B, Hornick JL. Giant Cell-Rich Tumors. In: *Practical Soft Tissue Pathology*. Philadelphia, PA: Elsevier; 2013:279-292.

4. Chow LT. Fibular giant cell-rich osteosarcoma virtually indistinguishable radiographically and histopathologically from giant cell tumor-analysis of subtle differentiating features. *Apmis*. 2015;123(6):530-539. doi:10.1111/apm.12382.

5. Yamamoto H, Iwasaki T, Yamada Y, et al. Diagnostic utility of histone H3.3G34W, G34R, and G34V mutant-specific antibodies for giant cel tumors of bone. *Human Pathology*. 2017.